# Drug Policy:
# Pegasys™ (peginterferon alfa-2a)

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|---|---|---|---|
| **POLICY NUMBER**<br>UM ONC_1497 | **SUBJECT**<br>Pegasys™ (peginterferon alfa-2a) | **DEPT/PROGRAM**<br>UM Dept | **PAGE 1 OF 5** |
| **DATES COMMITTEE REVIEWED**<br>04/10/24 | **APPROVAL DATE**<br>April 10, 2024 | **EFFECTIVE DATE**<br>April 26, 2024 | **COMMITTEE APPROVAL DATES**<br>04/10/24 |
| **PRIMARY BUSINESS OWNER:** UM | | **COMMITTEE/BOARD APPROVAL**<br>Utilization Management Committee | |
| **NCQA STANDARDS**<br>UM 2 | | **ADDITIONAL AREAS OF IMPACT** | |
| **CMS REQUIREMENTS** | **STATE/FEDERAL REQUIREMENTS** | **APPLICABLE LINES OF BUSINESS**<br>Commercial, Exchange, Medicaid | |

## I. PURPOSE

To define and describe the accepted indications for Pegasys (peginterferon alfa-2a) usage in the treatment of cancer, including FDA approved indications, and off-label indications.

Evolent is responsible for processing all medication requests from network ordering providers. Medications not authorized by Evolent may be deemed as not approvable and therefore not reimbursable.

The use of this drug must be supported by one of the following: FDA approved product labeling, CMS-approved compendia, National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO) clinical guidelines, or peer-reviewed literature that meets the requirements of the CMS Medicare Benefit Policy Manual Chapter 15.

## II. INDICATIONS FOR USE/INCLUSION CRITERIA

### A. Continuation requests for a not-approvable medication shall be exempt from this Evolent policy provided:

1. The member has not experienced disease progression on the requested medication AND
2. The requested medication was used within the last year without a lapse of more than 30 days of having an active authorization AND
3. Additional medication(s) are not being added to the continuation request.

### B. Myelofibrosis (PMF)

1. Pegasys (peginterferon alfa-2a) may be used as first line or subsequent therapy for members with low-risk myelofibrosis.

### Prognostic models for patients with PMF

| Prognostic model | Risk groups and clinical relevance |
|---|---|
| **IPSS**[80] | |
| Risk factors (weight): | Low risk: 0 (median survival, 11.3 y) |
| • Age >65 y (1 point) | Intermediate-1 risk: 1 point (7.9 y) |
| • Constitutional symptoms (1 point) | Intermediate-2 risk: 2 points (4.0 y) |
| • Hemoglobin <10 g/dL (1 point) | High risk: ≥3 points (2.3 y) |
| • WBC count >25 × $10^9$/L (1 point) | IPSS estimates survival at the time of diagnosis |
| • Circulating blasts ≥1% (1 point) | |
| **DIPSS**[81] | |
| Risk factors (weight): | Low risk: 0 (median survival, >20 y) |
| • Age >65 y (1 point) | Intermediate-1 risk: 1-2 points (14.2 y) |
| • Constitutional symptoms (1 point) | Intermediate-2 risk: 3-4 points (4.0 y) |
| • Hemoglobin <10 g/dL (2 points) | High risk: 5-6 points (1.5 y) |
| • WBC count >25 × $10^9$/L (1 point) | DIPSS can be applied anytime during clinical course |
| • Circulating blasts ≥ 1% (1 point) | |
| **DIPSS-plus**[83] | |
| Risk factors (weight): | Low risk: 0 (median survival, 15 y) |
| • DIPSS score (DIPPS low = 0, DIPPS int-1 = 1 point, DIPPS int-2 = 2 points, DIPSS high = 3 points) | Intermediate-1 risk: 1 point (6.6 y) |
| • RBC transfusion need (1 point) | Intermediate-2 risk: 2-3 points (2.9 y) |
| • PLT count <100 × $10^9$/L (1 point) | High risk: 4-6 points (1.3 y) |
| • Unfavorable karyotype* (1 point) | DIPSS-plus can be applied anytime during clinical course |

## C. Polycythemia Vera (PV)

1. Pegasys (peginterferon alfa-2a) may be used as first line or subsequent therapy for members with symptomatic low-risk polycythemia vera or high-risk polycythemia vera.


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**Table 5. Prognostic models for patients with PV**

| Prognostic model | Risk groups and clinical relevance |
|---|---|
| **Conventional thrombosis score (European LeukemiaNet recommendations)[70]** | |
| At least 1 of the following risk factors: | Low risk: age <60 y AND no history of thrombosis, that is, no risk factors |
| • Age ≥60 y | High risk: age ≥60 y AND/OR history of thrombosis, that is, at least 1 risk factor |
| • Previous thrombosis | Low-risk patients are given low-dose aspirin and undergo regular phlebotomy to keep hematocrit <45%; high-risk patients are given also a cytoreductive treatment |
| **IPSS for overall survival in PV[78]** | |
| Risk factors (weight): | Low risk: 0 (median survival, 28 y) |
| • Age ≥67 y (5 point) | Intermediate risk: 1-2 points (median survival, 19 y) |
| • Age 57-66 y (2 points) | High risk: ≥3 points (median survival, 11 y) |
| • Leukocyte count ≥15 × $10^9$/L (1 point) | |
| • Previous venous thrombosis (1 point) | |

### D. Essential Thrombocythemia (ET)

1. Pegasys (peginterferon alfa-2a) may be used as subsequent therapy for members with intermediate/high-risk essential thrombocythemia.

**Table 4. Prognostic models for patients with ET**

| Prognostic model | Risk groups and clinical relevance |
|---|---|
| **Conventional score for prediction of vascular complications (European LeukemiaNet recommendations)[70]** | |
| At least 1 of the following risk factors: | |
| • Age ≥60 y | Low risk: age <60 y AND no history of thrombosis or major bleeding AND PLT count <1500 × $10^9$/L, that is, none of the 3 major risk factors |
| • Previous thrombosis or major bleeding | High risk: age ≥60 y AND/OR history of thrombosis or major bleeding AND/OR PLT count ≥1500 × $10^9$/L, that is, at least 1 of the 3 major risk factors |
| • PLT count ≥1500 × $10^9$/L | While low-risk patients are just followed (observation alone) or given low-dose aspirin, high-risk patients are given a cytoreductive treatment plus low-dose aspirin |
| **IPSET-thrombosis (International Prognostic Score for ET: estimates the risk of thrombosis)[71]** | |
| Risk factors (weight): | Low risk: 0-1 point (probability of thrombotic events: 1.03% of patients/year) |
| • Age ≥60 y (1 point) | Intermediate risk: 2 points (2.35% of patients/year) |
| • Previous thrombosis (2 points) | High risk: ≥3 points (3.56% of patients/year) |
| • Cardiovascular risk factors* (1 point) | Potential therapeutic implications: (1) observation alone may be adequate in patients with no risk factors; (2) low-dose aspirin should be used in all patients with *JAK2* (V617F) and/or cardiovascular risk factors; (3) older patients (≥60 y) without additional risk factors may not need a cytoreductive treatment; (4) conversely, a cytoreductive treatment may be considered in younger patients (<60 y) with *JAK2*-mutant ET and concomitant cardiovascular risk factors, even in the absence of previous thrombosis |
| • *JAK2* (V617F) mutation (2 points) | |
| **IPSET (International Prognostic Score for ET: predicts survival)[73]** | |
| Risk factors (weight): | Low risk: 0 (median survival not reached) |
| • Age ≥60 y (2 points) | Intermediate risk: 1-2 points (median survival, 24.5 y) |
| • Previous thrombosis (1 point) | High risk: 3-4 points (median survival, 13.8 y) |
| • Leukocyte count >11 × $10^9$/L (1 point) | |

*Cardiovascular risk factors include hypertension, diabetes, and active tobacco use.

## III. EXCLUSION CRITERIA

A. Disease progression while taking Pegasys (peginterferon alfa-2a).

B. Concurrent use with other anticancer therapies.

C. Dosing exceeds single dose limit of 180 mcg.

D. Investigational use of Pegasys (peginterferon alfa-2a) with an off-label indication that is not sufficient in evidence or is not generally accepted by the medical community. Sufficient evidence that is not supported by CMS recognized compendia or acceptable peer reviewed literature is defined as any of the following:


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1. Whether the clinical characteristics of the patient and the cancer are adequately represented in the published evidence.
2. Whether the administered chemotherapy/biologic therapy/immune therapy/targeted therapy/other oncologic therapy regimen is adequately represented in the published evidence.
3. Whether the reported study outcomes represent clinically meaningful outcomes experienced by patients. Generally, the definitions of Clinically Meaningful outcomes are those recommended by ASCO, e.g., Hazard Ratio of < 0.80 and the recommended survival benefit for OS and PFS should be at least 3 months.
4. Whether the experimental design, considering the drugs and conditions under investigation, is appropriate to address the investigative question. (For example, in some clinical studies, it may be unnecessary or not feasible to use randomization, double blind trials, placebos, or crossover).
5. That non-randomized clinical trials with a significant number of subjects may be a basis for supportive clinical evidence for determining accepted uses of drugs.
6. That case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.
7. That abstracts (including meeting abstracts) without the full article from the approved peer-reviewed journals lack supporting clinical evidence for determining accepted uses of drugs.

## IV. MEDICATION MANAGEMENT

A. Please refer to the FDA label/package insert for details regarding these topics.

## V. APPROVAL AUTHORITY

A. Review – Utilization Management Department

B. Final Approval – Utilization Management Committee

## VI. ATTACHMENTS

A. None

## VII. REFERENCES


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